

Amendments to the Specification

Please amend the specification as follows:

Please replace the fourth full paragraph beginning on line 22 of page 2 with the words "In the immunological investigation..." with the following paragraph:

In the immunological investigation of synthetic glycopeptides which correspond to a tandem repeat of the MUC1 there it was surprisingly detected that the glycosylation of threonine in the immunodominant PDTRPAP (SEQ. ID NO: 3) region with α -GalNAc significantly increases the antigenicity. So far we proceeded on the theory that this position is not glycosylated in native MUC1, because it was assumed previously that, as a rule, glycosylation hindered the identification of peptide epitopes and the results of *in vitro* glycosylation experiments (Stadie. T. et al., Eur. J. Biochem. 229:1.40 (1995). Latest investigations (Mueller, S., et al., J. Biol. Chem. 272:24780, 1997), however, showed that threonine may be well glycosylated *in vivo* in the PDTRPAP (SEQ. ID NO: 3) variant. From these latest results the conclusion was drawn that the antigenicity (and in this connection also the immnogenicity) of the MUC1 tandem repeat will be significantly increased by glycosylating threonine in the PDTRPAP (SEQ. ID NO: 3) variant by means of GalNAc or by a short oligosaccharide. Thus, the immunogenic conformation of the immunodominant region is already reached by an individual tandem repeat. The antigenicity of the glycosylated PDTRPAP (SEQ. ID NO: 3) variant in a monorepeat exceeds even that of the oligomeric non-glycosylated peptide.

Please replace the first full paragraph beginning on line 11 of page 3 with the words "This discovery develops tumor vaccine..." with the following paragraph:

This discovery develops tumor vaccine mostly but not exclusively from human epithelial mucin MUC1 various molecular sizes glycosylated on threonine of the PDTRPAP (SEQ. ID NO: 3) variant by GalNAc, or a short oligosaccharide. That objective is met by synthetic peptides of various lengths, suitably a synthetic peptide having a length of at least 20

amino acids, and modified by human epithelial MUC1 glycosylated threonine and containing the immunodominant PDTRPAP (SEQ. ID NO: 3) region. The glycosylation can be suitably carried out by a monosaccharide, acetylgalactosamine (GalNAc), a short-chained oligosaccharide, and the disaccharide GalB-1, 3GalNAc.

Please replace the first full paragraph beginning on line 3 of page 4 with the words "In the following experiment..." with the following paragraph:

In the following experiment, the binding is investigated of monoclonal antibodies against the immunodominant PDTRPAP (SEQ. ID NO: 3) variant of the epithelial mucin to synthetic glycopeptides of this mucin in a solid-phase immunoassay (ELISA). The glycopeptides marked as A1 to A12 are indicated in the following Table. They correspond to an overlapping tandem repeat of MUC1 and contain 5 potential glycosylating sites (3 x threonine, 2 x serine); A1-A9 contains an additional alanine. The glycopeptides differ by the number and position of the glycosylating sites as specified in the Table. A1-A9 carry the Thomsen-Friedenreich (TF) antigen as glycan β -D-Gal(1-3) α -D-GalNAc-O-R whereas A11 and A12 carry only α -GalNAc-O-R (the Tn antigen). The antibodies used are: A76-A/C7 (mouse, IgG1, epitope: APDTRPAP (SEQ. ID NO: 3)) and MFO6 (mouse, IgG1, epitope: DTRPAP (SEQ. ID NO: 3)) (see: Rye, P.D., Price, M.R., eds., ISOBM TD-4 International Workshop on Monoclonal Antibodies against MUC1, Tumor Biol. 19, Suppl. 1, 1998).

Please replace the table beginning on line 5 of page 5 with the following table:

Table : Synthetic glycopeptides; the peptide corresponds to the basic structure of the epithelial mucin (MUC1). The immunodominant region is underlined as also shown in the drawing.

A: Glycosylation with TF:

A--H--G--V--T--S--A--P--D--T--R--P--A--P--G--S--T--A--P--P--A (SEQ. ID NO.: 1)
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21

Peptide # glycosylated in position:

A1	5
A2	10
A3	17
A4	6
A5	16
A6	5, 17
A7	5, 16, 17
A8	5, 6, 16, 17
A9	5, 6, 10, 16, 17

B: Glycosylation with Tn:

H--G--V--T--S--A--P--D--T--R--P--A--P--G--S--T--A--P--P--A (SEQ. ID NO.: 2)
2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21

Peptide # glycosylated in position:

All	5, 17
A12	5, 6, 10, 16, 17

Amendments to the Specification with Markings to Show Changes Made

The following paragraphs show the amendments made to certain paragraphs of the specification as set forth above. There are no newly added or entirely deleted paragraphs in this Amendment:

In the immunological investigation of synthetic glycopeptides which correspond to a tandem repeat of the MUC1 there it was surprisingly detected that the glycosylation of threonine in the immunodominant PDTRPAP (SEQ. ID NO: 3) region with α -GalNAc significantly increases the antigenicity. So far we proceeded on the theory that this position is not glycosylated in native MUC1, because it was assumed previously that, as a rule, glycosylation hindered the identification of peptide epitopes and the results of *in vitro* glycosylation experiments (Stadie, T. et al., Eur. J. Biochem. 229:1.40 (1995). Latest investigations (Mueller, S., et al., J. Biol. Chem. 272:24780, 1997), however, showed that threonine may be well glycosylated *in vivo* in the PDTRPAP (SEQ. ID NO: 3) variant. From these latest results the conclusion was drawn that the antigenicity (and in this connection also the immunogenicity) of the MUC1 tandem repeat will be significantly increased by glycosylating threonine in the PDTRPAP (SEQ. ID NO: 3) variant by means of GalNAc or by a short oligosaccharide. Thus, the immunogenic conformation of the immunodominant region is already reached by an individual tandem repeat. The antigenicity of the glycosylated PDTRPAP (SEQ. ID NO: 3) variant in a monorepeat exceeds even that of the oligomeric non-glycosylated peptide.

This discovery develops tumor vaccine mostly but not exclusively from human epithelial mucin MUC1 various molecular sizes glycosylated on threonine of the PDTRPAP (SEQ. ID NO: 3) variant by GalNAc, or a short oligosaccharide. That objective is met by synthetic peptides of various lengths, suitably a synthetic peptide having a length of at least 20 amino acids, and modified by human epithelial MUC1 glycosylated threonine and containing the

immunodominant PDTRPAP (SEQ. ID NO: 3) region. The glycosylation can be suitably carried out by a monosaccharide, acetylgalactosamine (GalNAc), a short-chained oligosaccharide, and the disaccharide GalB-1, 3GalNAc.

In the following experiment, the binding is investigated of monoclonal antibodies against the immunodominant PDTRPAP (SEQ. ID NO: 3) variant of the epithelial mucin to synthetic glycopeptides of this mucin in a solid-phase immunoassay (ELISA). The glycopeptides marked as A1 to A12 are indicated in the following Table. They correspond to an overlapping tandem repeat of MUC1 and contain 5 potential glycosylating sites (3 x threonine, 2 x serine); A1-A9 contain an additional alanine. The glycopeptides differ by the number and position of the glycosylating sites as specified in the Table. A1-A9 carry the Thomsen-Friedenreich (TF) antigen as glycan β -D-Gal(1-3) α -D-GalNAc-O-R whereas A11 and A12 carry only α -GalNAc-O-R (the Tn antigen). The antibodies used are: A76-A/C7 (mouse, IgG1, epitope: APDTRPAP (SEQ. ID NO: 3)) and MFO6 (mouse, IgG1, epitope: DTRPAP (SEQ. ID NO: 3)) (see: Rye, P.D., Price, M.R., eds., ISOBM TD-4 International Workshop on Monoclonal Antibodies against MUC1, Tumor Biol. 19, Suppl. 1, 1998).

Table : Synthetic glycopeptides; the peptide corresponds to the basic structure of the epithelial mucin (MUC1). The immunodominant region is underlined as also shown in the drawing.

A: Glycosylation with TF:

A--H--G--V--T--S--A--P--D--T--R--P--A--P--G--S--T--A--P--P--ASEQ. ID NO.: 1
 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21

Peptide # glycosylated in position:

A1 5

A2 10

A3	17
A4	6
A5	16
A6	5, 17
A7	5, 16, 17
A8	5, 6, 16, 17
A9	5, 6, 10, 16, 17

B: Glycosylation with Tn:

H	--	G	--	V	--	T	--	S	--	A	--	<u>P</u>	--	<u>D</u>	--	<u>T</u>	--	<u>R</u>	--	<u>P</u>	--	<u>A</u>	--	<u>P</u>	--	G	--	S	--	T	--	A	--	P	--	P	--	A	SEQ. ID NO.: 2	
2		3		4		5		6		7		8		9		10		11		12		13		14		15		16		17		18		19		20		21		

Peptide # glycosylated in position:

All	5, 17
A12	5, 6, 10, 16, 17